REMARKS/ARGUMENTS

Claims 1-11, 19, and 26-31, 33, and 34-38 are pending in the application. In response thereto, Applicant has amended Claims 1, 9, 34, 36, and added new Claim 39. No new matter has been added.

A. Objections to the Drawings

On page 2 of the Office Action, the Examiner objected to the drawings because the figure does not identify the data points corresponding to donation per the description. Applicant is submitting corrected drawings in a separate paper under 37 C.F.R. § 1.121(d) in accordance with the Examiner's suggestions. No new matter has been added. Withdrawal of the objection to the drawings is respectfully requested.

B. Claim Objections

On page 3 of the Office Action, the Examiner objected to Claim 34 as containing typographical errors. Applicant has corrected Claim 34 in accordance with the Examiner's suggestions. Withdrawal of the objection is respectfully requested.

C. Indefiniteness

On page 3 of the Office Action, the Examiner rejected Claims 1-11, 26-31, 33, and 36 under 35 U.S.C. § 112 ¶ 2 as being indefinite. More specifically, the Examiner rejected Claim 1 as having insufficient antecedent basis for "the wound site." In response, Applicant has amended Claim 1 to refer to "a wound site." Withdrawal of the rejection is respectfully requested.

In addition, on pages 3-4 of the Office Action, the Examiner rejected Claims 9 and 36 as being vague and indefinite. In response, Claim 9 has been amended to clarify the limit of the LAL test. The Examiner rejected Claim 36, and stated that it was unclear to what the microbial

cellulose was exposed to at 30 to 100 °C for about 1 to 4 hours. As noted in Paragraph 0040 of the present application, the microbial cellulose pellicles are exposed to the recited temperatures in order to purify the pellicles and render them nonpyrogenic. Applicant has amended Claim 36 to better clarify this, and withdrawal of the rejections is respectfully requested.

D. Obviousness

On pages 4-8 of the Office Action, the Examiner rejected Claims 1-4, 9-11, 19, 26-31, 33-34, and 37-38 as being obvious in view of Ring et al., US Patent No. 4,588,400 ("the Ring '400 Patent"). Applicant notes that the Examiner did not reject Claims 5-8 and 36 as being obvious based on the Ring '400 Patent. Thus, Applicant has submitted new Claim 39 directed to the subject matter of Claims 5-8. Further, Applicant traverses the rejection as to the claims.

1. The Ring '400 Patent Does not Teach or Suggest 1.5 to 4.5% Microbial Cellulose for both Donation/Absorption as Recited in Claims 1-4, 9-11, 19, 26-31, 33-34, and 37-38.

Independent Claim 1 (and new Claim 39) are directed to a method for treating chronic wounds using a kit comprising a microbial cellulose dressing consisting essentially of 1.5% to 4.5% microbial cellulose and water. The ability of the dressing to donate greater than 75% of its liquid weight and also absorb liquid in an effective amount for the treatment of chronic wounds is also claimed. Likewise, independent Claims 19 and 37 is directed to a method for preparing a wound dressing consisting essentially of 1.5% to 4.5% microbial cellulose and water which has the claimed donation/absorption ability. Independents Claim 34 is directed to an improved method of treating chronic wounds using a wound dressing consisting essentially of 1.5% to 4.5% microbial cellulose and water,, which reduces pain compared to prior art non-adhesive gauze dressings.

In this case, the Ring '400 Patent broadly teaches a liquid loaded pad having a weight ratio of liquid to cellulose from about 5:1 to 150:1 (Claim 2) – which corresponds to a range of 0.7 to 17 wt.% cellulose – and wherein the liquid is distilled water, saline, glycerol, polyethylene glycol, lower alcohols, and mixtures thereof (Claim 3). Thus, the Ring '400 Patent contemplates liquid loaded pads having a very wide range of cellulose contents and a very wide range of liquid types in the liquid loaded pad. As FIG. 1 of the present application shows, liquid loaded pads having very low (*e.g.*, 0.7 wt.%) and very high (*e.g.*, 20 wt.%) cellulose contents are unable to both donate and absorb liquid essential for treating non-responsive chronic wounds as claimed. As discussed more fully below, none of the examples in the Ring '400 Patent fall within the claimed cellulose content range and the claimed liquid type (water). As such, Applicant respectfully submits that the claimed invention is not obvious in view of the Ring '400 Patent.

Example 1 of the Ring '400 Patent teaches a saturated cellulose pellicle comprising 40 g/M^2 cellulose and 3600 g/M^2 water. This corresponds to a cellulose content of 1.1 wt.% cellulose.[1] Example 1 does not render the claimed invention obvious for at least three reasons. First, the cellulose content of Example 1 is outside the claimed range of 1.5 to 4.5 wt.% cellulose. Second, FIG. 1 of the present application shows that such low cellulose values (near 1%) are unable to both donate and absorb liquid as claimed. Third, the Ring '400 Patent provides no evidence that the liquid loaded pads may successfully treat non-responsive chronic wounds (*see* Part D(2) below) Thus, Applicant respectfully suggests that the claimed invention is not obvious in view of Example 1 of the Ring '400 Patent.

Example 2 of the Ring '400 Patent teaches a water loaded pellicle having a water to cellulose ratio of 8:1, which corresponds to 11.1 wt.% cellulose. This is well outside the claimed

[1] The calculation is (40 g/M^2)/(40 g/M^2 + 3600 g/M^2) or 1.1 wt.%.

range of 1.5 to 4.5 wt.% cellulose. Example 2 prophetically describes a water-loaded pellicle having a liquid to cellulose content ranging from 2:1 to 20:1 that "may be prepared" (column 5, line 38). This corresponds to 33% to 4.8% wt.% cellulose. Again, this is outside the claimed range. Further, there is no teaching that such a dressing can be used for the effective treatment of a chronic wound as claimed.

Examples 3-8 of the Ring '400 Patent either recite processing conditions that make it difficult to calculate the cellulose content, have cellulose contents clearly outside the claimed range, or include chemicals (such as glycerol, polyethylene glycol, or petrolatum) that negatively affect performance of the product if used as a chronic wound dressing.

More specifically, Example 3 of the Ring '400 Patent teaches a sheet according to Example 2 (*i.e.*, a water-to-cellulose ratio of 8:1 or 11 wt.% cellulose) immersed in water, water/glycerol, or saline, in which "about 70% of the original liquid content" was recovered. Thus, the liquid content in Example 3 is actually decreased by 30% so that the ratio is 5.6 to 1 (70% x 8:1), which corresponds to 15 wt.% cellulose. Again, this is outside the claimed range such that Example 3 does not render the claimed invention obvious.

Example 4 of the Ring '400 Patent teaches a sheet material reconstituted with glycerol or polyethylene glycol ("PEG") to obtain a liquid content of 2000 g/M^2 liquid and 40 g/M^2 cellulose (from Example 1) or a liquid to cellulose ratio of 50:1. Thus, the resulting material had a cellulose content of 2 wt.% and water and glycerol or PEG. Importantly, the claimed invention is limited to a wound dressing "consisting essentially" of microbial cellulose and water. As set forth in the previously submitted Damien Declaration under § 1.132 (previously submitted in the response filed on February 11, 2008, attached as Exhibit F), Applicant has conducted

experiments to show that the claimed invention has donative/absorptive properties superior to that of Examples 4, 7, and 8 of the Ring '400 Patent.

Example 5 of the Ring '400 Patent teaches air drying the pellicle and then immersing the sheet in glycerol where it regains about 5% of its original liquid content. Five percent of 3600 g/M^2 is 180 g/M^2. Thus, the resulting material comprised 40 g/M^2 cellulose and 180 g/M^2 glycerol or about 18 wt.% cellulose. Thus, the claimed invention is not obvious in view of Example 5 of the Ring '400 Patent because the cellulose content is well outside the claimed range.

Example 6 of the Ring '400 Patent teaches reconstituting the sheet material with polyvinylpyrolidone ("PVP") to about 70% of its original liquid content. The pellicle was then allowed to air dry to about 50% of its reconstituted weight. The pellicle was then exposed to an electron beam to cross link the PVP to form a gel within the pellicle. Thus, Example 6 of the Ring '400 Patent does not render the claimed invention obvious because it teaches a PVP cross-linked "gel" in the dressing and does not "consist essentially of" water and microbial cellulose as claimed.

Example 7 of the Ring' 400 patent teaches reconstituting the sheet material with 1% silver sulfadiazine ("SSD") ointment. The liquid content increased to about 1000 g/M^2. Thus, the resulting material comprised 40 g/M^2 cellulose and 1000 g/M^2 liquid (water and SSD) or about 3.8% cellulose. As set forth in the Damien Declaration, Applicant has conducted experiments to show that the claimed invention has donative/absorptive properties superior to that of Examples 4, 7, and 8 of the Ring '400 Patent.

Example 8 of the Ring '400 Patent teaches reconstituting the sheet material with water to 2000 g/M^2 and then immersing the pellicle in petrolatum. Thus, the resulting material comprised

40 g/M^2 cellulose and 2000 g/M^2 liquid (water and petrolatum) or about 2% cellulose. The resulting product was a petroleum-coated dressing having a water core. As set forth in the Damien Declaration, Applicant has conducted experiments to show that the claimed invention has donative/absorptive properties superior to that of Examples 4, 7, and 8 of the Ring '400 Patent.[2]

In short, none of the examples in the Ring '400 Patent discloses a method of treating chronic wounds with a microbial cellulose dressing consisting essentially of 1.5 to 4.5 wt.% cellulose that is capable of both absorbing and donating liquid in the amount claimed. In dressings with less than 1.5 wt.% microbial cellulose, the dressing fails to absorb significant amounts of exudates from a chronic wound. With amounts more than 4.5 wt.% microbial cellulose, the dressing fails to hydrate the wound bed adequately. The dressings in the examples describe only examples which either absorb (highest cellulose range) or hydrate (lowest cellulose range) – but not both. *See* column 3, lines 29-31 ("either supply moisture to the wound or absorb exudate"). The claimed dressing is capable of donating about 75% to 95% of its liquid weight and is also is capable of absorbing between about 35% to 75% of its liquid weight where the wound has exudates. *See* FIG. 1. These properties were not recognized in the prior art and are critical in the treatment of chronic wounds.

2. The Ring '400 Patent Does not Teach or Suggest the Treatment of Chronic Wounds Microbial Cellulose in Claims 1-4, 9-11, 19, 26-31, 33-34, and 37-38.

[2] Applicant respectfully submits that Example 8 actually teaches away from the "method of treatment" claims of the present invention. That is, Example 8 teaches only that the final petrolatum-coated product should be applied as a treatment for acute wounds, not the intermediate product. In contrast, the present invention is directed to a method of treating chronic wounds with a microbial cellulose dressing consisting essentially of from 1.5% to about 4.5% cellulose and water. Moreover, in order to clarify that the intermediate product is excluded from the claim scope, Claims 1, 19, and 39 recite that the microbial cellulose dressing is placed in a moisture-proof package and instructions are provided concerning placement on a chronic wound.

Independent Claims 1 and 34 are directed to a method for treating chronic wounds. Claim 34 emphasizes the reduction in pain compared to prior art gauze dressings as described in Example 5 (Paragraphs 0059-0069 of the patent application). In addition, independent Claim 19 includes providing instructions for applying the microbial cellulose dressing to a chronic wound. Applicant respectfully submits that the claimed method of treating a specific type of wound – non-responsive chronic wounds in humans – is non-obvious in view of the Ring '400 Patent.

The Ring '400 Patent only mentions the possibility of treating ulcers hypothetically with liquid loaded pads having an occlusive film. *See* column 9, lines 24-50 ("A dressing ....may be applied to such an ulcer..."). Yet, the Ring '400 Patent does not specify what type of ulcers are contemplated. Nor is there any evidence of healing success in treatment of non-responsive chronic wounds over a long period of time. The only biological data disclosed in the Ring' 400 Patent deals with the use of the liquid loaded pad from Example 4 (which contained PEG or glycerol) in guinea pig studies in which the full thickness of skin in the dorsal area was surgically removed. *See* column 7, line 60 to column 8, line 4. Further, the Ring '400 Patent only investigated treatment for 8 days. Clearly, this type of "surgical wound" is an acute wound and not a chronic wound as claimed. A chronic wound is a non-responsive wound that has failed to proceed through an orderly and timely process to produce anatomic and functional integrity, or one that has proceeded through the repair process without establishing a sustained anatomic and functional result. *See* Lazarus et al., *Definitions and Guidelines for Assessment of Wounds and Evaluation of Healing*, Arch Dermatol. 130:489-493, at page 490 (1994) (previously submitted in the response filed on February 11, 2008, attached as Exhibit A). For these additional reasons, Applicant respectfully submits that the claimed invention is non-obvious in view of the Ring '400 Patent.

In addition, in Davis et al., *Wound environment: implications from research studies for healing and infection*, Krasner DL, Rodehaver GT, Sibbald RG eds. CHRONIC WOUND CARE: A CLINICAL SOURCE BOOK FOR HEALTHCARE PROFESSIONALS (4th ed. Malvern, Pa: HMP Communications), pages 205-213 (2007) (previously submitted in the response filed on February 11, 2008, attached as Exhibit B) the authors recognized that "small mammal[s] (*e.g.*, mouse, rabbit, guinea pig)... have striking differences to humans [since] they tend to have dense fur with relatively thin epidermal and dermal layers. Additionally, they heal mostly by wound contraction instead of re-epithelization." *See* page 205 line 14. Therefore, treating non-responsive chronic wounds in humans is not rendered obvious by the Ring '400 Patent, which contains only animal data for acute surgical wounds.

The literature also shows that different kinds of wounds require different kinds of dressings depending on their history and development. *See* Broussard, *Dressing Decisions*, Krasner DL, Rodehaver GT, Sibbald RG eds. CHRONIC WOUND CARE: A CLINICAL SOURCE BOOK FOR HEALTHCARE PROFESSIONALS (4th ed. Malvern, Pa: HMP Communications), pages 249-262 (2007) (previously submitted in the response filed on February 11, 2008, attached as Exhibit C). Therefore, Applicant respectfully submits that it is not obvious to apply dressings that the prior art teaches may be used on acute wounds over a relatively short period of time on non-responsive chronic wounds as in the present invention.

In short, Applicant respectfully submits that one skilled in the art would not equate the treatment of an 8-day-old "acute wound" of the Ring '400 Patent with the treatment of non-responsive chronic wounds as claimed. Because the claimed invention is able to both absorb and donate more than 75% of its weight of liquid, improved healing of chronic wounds is possible

compared to that found in the prior art. For this additional reason, Applicant respectfully submits that the claimed invention is not obvious in view of the Ring '400 Patent.

In the present invention, the microbial cellulose dressings having 1.5 to 4.5 wt.% cellulose were used to treat non-responsive chronic wounds. This had not been done before such that the claimed invention is non-obvious. The specification states in part:

> Example 4
>
> Human Clinical Effectiveness Testing in Treating Chronic Wounds
>
> [0057] The objective of the human clinical testing was to assess the effectiveness of the cellulose wound dressing in treating various types of chronic wounds. A total of 29 patients with 31 various types of chronic wounds were involved in the study. The patients were treated with the cellulose wound dressing after passing the inclusion criteria outlined in the study protocol approved by an institutional review board (IRB). The cellulose wound dressing treatment was implemented for eight weeks or until the wound healed. Weekly wound observations were conducted. After the observations were recorded the dressings were changed. Both wound condition and size were recorded during the weekly visits and the study was terminated after the wounds healed or eight weeks of treatment.
>
> [0058] The results of the human study can be divided into three notable indications based on the performance of the cellulose wound dressing. The cellulose wound dressing exhibited strength in the removal of slough necrosis in deep pressure ulcers. Application of the cellulose wound dressing reduced the hypergranulation tissue down to the level of the surrounding epithelium in two wound presented with the problem. The third and most interesting response to the cellulose wound dressing was observed during the treatment of venous leg ulcers, particularly those with full thickness tissue involvement. The results showed that out of thirteen (13) venous leg ulcers (two partial thickness and eleven full thickness wounds), seven (54%) were completely healed and the remainder (46%) showed improvement during the course of the eight-week study.

See Paragraph 0057-0058 (emphasis added). This clinical study was further detailed in Example 5 (Paragraphs 0059 to 0072) and Brown-Etris et al., *Evaluation of XCell Wound Dressing on Wound Healing of Pressure Ulcers* (2003) (attached as Exhibit D) and Brown-Etris et al.,

Evaluation of XCell Wound Dressing on Wound Healing of Venous Stasis Ulcers (2003) (attached as Exhibit E).

With respect to pressure ulcers, FIGs. 6-15 of Exhibit D (previously submitted) describe how treatments prior to the use of XCell® wound care dressing included mechanical, chemical, and autolytic debridement and use of other wound dressings. Therefore, the success of XCell® (14 of 16 evaluable wounds; Table 1) in showing healing or improvement over the eight-week treatment was truly unexpected and further demonstrates that success in medical arts, especially in wound healing, is not as predictable as in mechanical arts.

Similarly, with respect to venous ulcers, FIGs. 4-6 of Exhibit E (previously submitted) show the "[h]ealing of a venous ulcer [that was] classified as a non-responsive wound that had lasted one to three months. Previous treatments included mechanical debridement and use of other wound dressings. Over the study, the wounds continued to heal [...] to being fully healed at six weeks." Also, FIGs. 7-9 and FIGs. 10-11 demonstrate the unexpected success of XCell® quite strongly.

Importantly, a particular parameter must first be recognized as a result-effective variable, *i.e.*, a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 U.S.P.Q. 6 (CCPA 1977) (The claimed wastewater treatment device had a tank volume to contractor area of 0.12 gal./sq. ft. The prior art did not recognize that treatment capacity is a function of the tank volume to contractor ratio, and therefore the parameter optimized was not recognized in the art to be a result- effective variable.). Applicant respectfully submits that there is no teaching or suggestion in the Ring '400 Patent that the amount of cellulose in the wound dressing "consisting essentially of" 1.5 to 4.5% cellulose and

water would be capable of donating greater than 75% of its liquid weight to a dry or necrotic portion of a chronic wound and absorbing liquid in an amount effective for treatment of a chronic wound. The Ring '400 Patent is absolutely silent in suggesting that one could control absorption and donation as claimed, and to achieve a proper balance of the two through selection of the right amount of cellulose and water to lead to a dressing for the treatment of chronic wounds. The Ring '400 Patent teaches a broad range of cellulose contents, water contents in combination with other ingredients, such as glycerol, PVP, sulfadiazine, and petrolatum. Indeed, as discussed above and in the declarations, such ingredients interfered with the ability of the dressing to absorb/donate water as claimed.

For all of these reasons, Applicant respectfully requests that the claimed invention is not obvious based on the Ring '400 Patent.

E. Double Patenting

On pages 8-14, the Examiner rejected the pending claims as being subject to obviousness-type double patenting based on Applicant's co-pending applications. In particular, on page 9, the Examiner rejected Claims 1-11, 19, 33, and 37-38 as subject to non-statutory obviousness-type double patenting based on Claims 1-11 of U.S. Patent No. 7,390,499. On pages 10-11, the Examiner rejected Claims 1-11, 19, 16-31, 33, and 36-38 as subject to non-statutory obviousness-type double patenting based on Claims 1-10, 18 and 25-28 of co-pending U.S. Patent No. Serial No. 10/173,576. On page 12, the Examiner rejected Claims 1-4 and 9-11 as subject to non-statutory obviousness-type double patenting based on Claims 1, 16-17, and 26-27 of co-pending U.S. Patent No. Serial No. 10/345,394. On page 13, the Examiner rejected Claims 1-11, 19, 26-31, and 33-34 as subject to non-statutory obviousness-type double patenting based on Claims 13 and 45-40 of co-pending U.S. Patent No. Serial No. 10/425,978.

Enclosed herewith is a Terminal Disclaimer to Obviate a Double Patenting Rejection Over a "Prior" Patent and three Terminal Disclaimers to Obviate a Provisional Patenting Rejection Over a Pending "Reference" Application, along with the requisite fees. Applicant believes that the disclaimers overcome the examiner's rejection of all of the claims on the basis of obviousness-type double patenting. Withdrawal of the rejection is expressly requested.

In view of the foregoing amendments and remarks, it is respectfully submitted that the claims are now in condition for allowance and eventual issuance. Such action is respectfully requested. Should the Examiner have any further questions or comments which need be addressed in order to obtain allowance, please contact the undersigned attorney at the number listed below.

Acknowledgement of receipt is respectfully requested.

Respectfully submitted,

By: _____

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